DOI: 10.4274/turkderm.galenos.2025.02696
Turkderm-Turk Arch Dermatol Venereol 2025;59(3):103-104

Adalimumab treatment for lower extremity ulcers associated with prolidase deficiency

Prolidaz eksikliğiyle ilişkili alt ekstremite ülserleri için adalimumab tedavisi

Hanife Uçgun Demirtaş*, Büşra Özkan Çalışkan*, Selami Aykut Temiz*, Mahmut Selman Yıldırım, Recep Dursun***

*Necmettin Erbakan Univercity Medical Faculty, Department of Dermatology, Konya, Türkiye
**Necmettin Erbakan Univercity Medical Faculty, Department of Medical Genetics, Konya, Türkiye

Keywords: Prolidase deficiency, anti-TNF, adalimumab, lower extremity ulcers

Anahtar Kelimeler: Prolidaz eksikliği, anti-TNF, adalimumab, alt ekstremite ülserleri

Dear Editor,

Prolidase deficiency (PD) is an autosomal recessive disorder that leads to impaired collagen degradation[1]. Prolidase is a common cytosolic dipeptidase that releases proline or hydroxyproline in the final stage of endogenous and dietary protein catabolism. Prolidase contributes to the cycle of collagen and other proline-containing proteins[2]. Among the many clinical manifestations of PD are dysmorphic facial features, skeletal deformities, hepatosplenomegaly, necrotizing skin ulcers, and recurrent infections. Current clinical knowledge of this genetic disease is based on a limited number of case reports owing to its extremely rare nature. Diagnosis relies on identifying a pathogenic gene variant[1].

We present a case of a 27-year-old woman with a 16-year history of bilateral non-healing ulcers on the feet, accompanied by splenomegaly and a history of recurrent lung infections. We highlight the consideration of PD in the differential diagnosis of leg ulcers with this rare case and present the successful treatment outcome of adalimumab therapy in the management of resistant ulcers associated with PD.

The 27-year-old female patient had a history of first-degree consanguinity in her family, with no other individuals in the pedigree exhibiting similar complaints. Since the age of 11, she has experienced ulcers on her feet and recurrent lung infections. Physical examination revealed multiple ulcers with raised edges on the lateral and dorsal aspects of the feet (Figure 1a). Prominent findings included frontal bossing, mild exophthalmos, saddle nose, and hypertelorism. Laboratory tests, including complete blood count, serum electrolytes, urea, creatinine, creatinine kinase, liver function tests, IgA, IgG, IgM, IgE, and autoimmune markers (ANA, ANCA, anti-dsDNA), as well as hemoglobin electrophoresis, were normal. Thoracic computed tomography and high-resolution computed tomography revealed bronchiectasis and pneumonic consolidation. Arterial and venous Doppler ultrasonography revealed no abnormalities. Magnetic resonance angiography demonstrated flow in the anterior-

Address for Correspondence/Yazışma Adresi: Selami Aykut Temiz Assoc. Prof., Necmettin Erbakan Univercity Medical Faculty, Department of Dermatology, Konya, Türkiye
E-mail: aykutmd42@gmail.com **ORCID:** orcid.org/0000-0003-4878-0045

Received/Geliş Tarihi: 01.08.2024 **Accepted/Kabul Tarihi:** 03.09.2025 **Publication Date/Yayınlanma Tarihi:** 30.09.2025

Cite this article as/Atıf: Demirtaş HU, Çalışkan BÖ, Temiz SA, Yıldırım MS, Dursun R. Adalimumab treatment for lower extremity ulcers associated with prolidase deficiency. Turkderm-Turk Arch Dermatol Venereol. 2025;59(3):103-104

Turkderm - Turk Arch Dermatol Venereol
2025;59(3):103-104

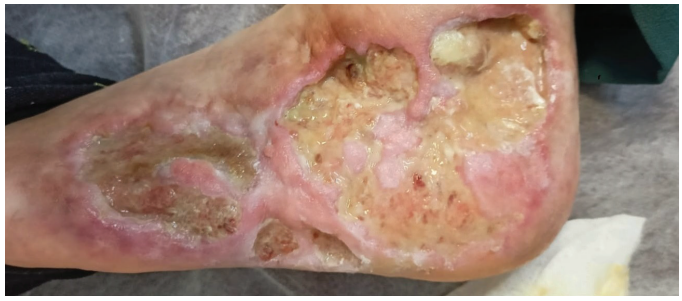

Figure 1a. Widespread ulcers before adalimumab treatment

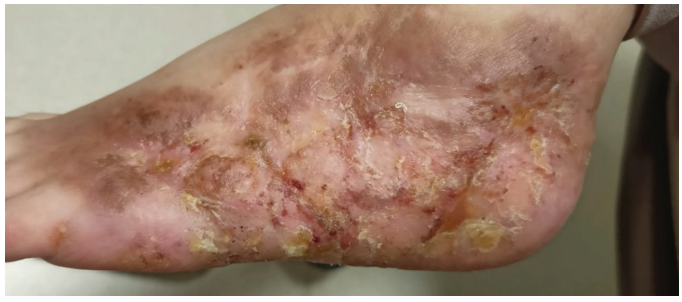

Figure 1b. After adalimumab treatment

posterior, tibial, and peroneal arteries of the left thigh, with occasional stenosis and irregularities in the arterial structures. Abdominal ultrasonography revealed a normal liver with splenomegaly. Skin biopsy revealed non-specific findings. The patient had been followed up in the rheumatology department for over 10 years with provisional diagnoses of scleroderma, vasculitis, and pyoderma gangrenosum. The patient was treated for a prolonged period with topical epithelizing agents, topical antibiotics, topical tacrolimus, intermittent oral antibiotics for 10 years, oral prednisolone for 6 years, subcutaneous methotrexate for 7 years, oral colchicine for 7 years, and oral iloprost for 1 year without a satisfactory response. Adalimumab therapy was added to colchicine 0.5 mg twice a day. Adalimumab treatment was initiated with off-label approval from the Ministry of Health and with the patient's verbal and written consent. The patient was referred for genetic counseling, accompanied by her clinical history. Genetic testing revealed the homozygous presence of the PEPD (ENST00000244137): c.876del p.(Ala294ProfsTer27) variant, leading to a diagnosis of PD. During this period, the patient responded to adalimumab, and by the end of the 11th month, the lesions on her feet had healed (Figure 1b). No side effects were observed during the patient's one-year-long adalimumab treatment. Written and verbal informed consent was obtained from the patient for this article.

PD is associated with a broad range of dermatological symptoms. Overall, 61% of patients are characterized by skin ulcers[2]. There is no established treatment for PD. Despite various topical, systemic, and surgical treatments described in the literature for leg ulcers associated with PD, there is currently no definitive therapeutic approach or established standard of care[3]. The treatment methods include oral proline, manganese, ascorbic acid supplements, glycine, and proline topical application; topical and subcutaneous growth hormone; oral dapsone; transfusion of normal erythrocytes; plasmapheresis; skin grafting; high-dose pulsed systemic steroids; and pentoxifylline[4].

We report the successful treatment of PD ulcers with adalimumab. Adalimumab was chosen for its antifibrotic effects and efficacy in treating other ulcerative diseases. TNF-α plays a central role in chronic inflammatory processes and impaired wound healing. Adalimumab binds to TNF-α and neutralizes its biological activity, thereby reducing inflammation and promoting ulcer healing[5]. In our case of resistant ulcers diagnosed with PD, we administered adalimumab subcutaneously at a dose of 80 mg/week for the first 2 weeks, followed by 40 mg/week. Partial improvement was observed at the 3-month mark, with dramatic healing of the lesions on the feet by the 11th month. The clinical success of this anti-inflammatory treatment may be consistent with the proposed pathological mechanisms of PD, as prolidase is involved in inflammatory signaling pathways that play a role in collagen turnover and matrix degradation[3]. Further large-scale studies are needed to confirm this success, but adalimumab should be considered in the management of PD ulcers.

Ethics

Informed Consent: Written and verbal informed consent was obtained from the patient for this article.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ido F, Tessier S, Yoder N, Ramzy J, Longo S: Prolidase deficiency: A novel PEPD missense variant in exon 2. Am J Med Genet A. 2023;191:1388-94.
2. Spodenkiewicz M, Spodenkiewicz M, Cleary M, et al: Clinical genetics of prolidase deficiency: an updated review. Biology (Basel). 2020;9:108.
3. Good AJ, Nielson CB, Schoch JJ: Topical tacrolimus therapy in the management of lower extremity ulcers due to prolidase deficiency. Pediatr Dermatol. 2019;36:926-8.
4. Adışen E, Erduran FB, Ezgü FS, et al: A rare cause of lower extremity ulcers: Prolidase deficiency. Int J Low Extrem Wounds. 2016;15:86-91.
5. Ellis CR, Azmat CE: Adalimumab. 2023 Nov 12. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.